ORIGINAL ARTICLES

Presentations of Acute Myocardial Infarction in Men and Women

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OBJECTIVE: **To assess the influence of gender on the likelihood of acute myocardial infarction (AMI) among emergency department (ED) patients with symptoms suggestive of acute cardiac ischemia, and to determine whether any specific presenting signs or symptoms are associated more strongly with AMI in women than in men.**

DESIGN: **Analysis of cohort data from a prospective clinical trial.**

SETTING: **Emergency departments of 10 hospitals of varying sizes and types in the United States.**

PATIENTS: **Patients 30 years of age or older (n = 10,525) who presented to the ED with chest pain or other symptoms suggestive of acute cardiac ischemia.**

MEASUREMENTS AND MAIN RESULTS: **The prevalence of AMI was determined for men and women, and a multivariable logistic regression model predicting AMI was developed to adjust for patients' demographic and clinical characteristics. AMI was almost twice as common in men as in women (10% vs 6%). Controlling for demographics, presenting signs and symptoms, electrocardiogram features, and hospital, male gender was a significant predictor of AMI (odds ratio [OR] 1.7; 95% confidence interval [CI] 1.4, 2.0). The gender effect was eliminated, however, among patients with ST-segment elevations on electrocardiogram (OR 1.1; 95% CI 0.7, 1.7) and among patients with signs of congestive heart failure (CHF) (OR 1.1; 95% CI 0.8, 1.5). Signs of CHF were associated with AMI among women (OR 1.9; 95% CI 1.4, 2.6) but not men (OR 1.0; 95% CI 0.8, 1.3). Among patients who presented to EDs with chest pain or other symptoms suggestive of acute cardiac ischemia, AMI was more likely in men than in women. Among women with ST-segment elevation or signs of CHF, however, AMI likelihood was similar to that in men with these characteristics.**

KEY WORDS: **emergency department (ED); presentation; acute myocardial infarction (AMI); gender; congestive heart failure (CHF).**

J GEN INTERN MED 1997;12:79–87.

The benefits of time-dependent therapeutic interventions for acute myocardial infarction (AMI) depend on prompt and accurate diagnosis of AMI by emergency department (ED) physicians. As aids to rapid identification, risk factors, presenting characteristics, and diagnostic test results have been related to the occurrence of AMIs.[1–7] These can help in assessing a patient's likelihood of AMI, but their predictive value may differ for certain subgroups of patients.[4,8–10] In particular, gender may significantly affect the likelihood of AMI in ED patients with chest pain or other symptoms of acute cardiac ischemia.

The incidence of AMI in the general population has been shown to be higher in men than women,[11–14] but it is not clear whether this gender difference holds among symptomatic patients who come to the ED. Knowing whether gender influences the likelihood that a given ED patient is having an AMI and whether any specific presenting signs and symptoms are differentially associated with AMI in women as compared with men could aid ED physicians in the accurate diagnosis of AMI.

Several studies have looked at gender differences in the presentation of patients with AMI.[15–19] In a retrospective analysis of patients with confirmed AMI, women had higher rates of atypical presentations such as abdominal pain, paroxysmal dyspnea, or congestive heart failure (CHF).[11,20–23] In a group of ED patients with typical presentations such as chest pain, the prevalence of AMI was lower in women.[2,24] However, in another study of ED patients with chest pain, when adjustments were made for other presenting clinical features (specifically electrocardiographic findings), the gender difference was no longer significant.[18] From these results it is difficult to assess whether the gender-specific differences in AMI prevalence among symptomatic ED patients were the result of gender-specific biology or limitations in a particular study's patient selection.

Received from the Center for Cardiovascular Health Services Research, Division of Clinical Care Research, Department of Medicine, New England Medical Center and Tufts University School of Medicine, Boston, Mass.

Presented at the American Federation of Clinical Research meeting, May 1995, and the National Research Service Award Trainees Research Conference, June 1995.

Supported in part by Agency for Health Care Policy and Research grants T32 HS00060 and R01 HS07360 and by National Heart, Lung and Blood Institute grant R01 HL53900.

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To address these uncertainties, we used data from a large prospective, multicenter clinical trial, the Acute Cardiac Ischemia Time-Insensitive Predictive Instrument (ACI-TIPI) Trial, of patients who presented to EDs with chest pain or with other more atypical presentations suggestive of acute cardiac ischemia.[25] We hypothesized that among these ED patients gender was a significant predictor of AMI even after controlling for presenting characteristics that are commonly associated with AMI. Furthermore, we considered that there might be presenting characteristics which are differentially associated with AMI in women as compared with men. To test these hypotheses, we assessed the prevalence of AMI among men and women in the ED, and looked for gender-specific differences in the clinical presentations of patients with AMI.

METHODS

Patient Inclusion

Study subjects were participants in the ACI-TIPI Trial,[25] a prospective trial carried out over a 7-month period starting May 1993 at 10 hospitals of varying sizes and types: Baystate Medical Center (Springfield, Mass.), Boston (Mass.) City Hospital, Boston (Mass.) University Medical Center, Medical College of Virginia (Richmond), Medical College of Wisconsin (Milwaukee), New England Medical Center (Boston, Mass.), Newton-Wellesley Hospital (Newton, Mass.), Rhode Island Hospital (Providence), University of Cincinnati (Ohio) Medical Center, and University of North Carolina (Chapel Hill) Hospital.

Informed consent was requested of all patients presenting to the ED if they were 30 years of age or older and their reasons for coming to the ED included chest pain (including chest pressure or discomfort), arm pain, jaw pain or other equivalent discomfort, epigastric discomfort suggestive of acute cardiac ischemia, shortness of breath, dizziness, palpitations, syncope, or other symptoms suggestive of cardiac ischemia. Of all eligible patients 92% consented and were enrolled in the study (N = 10,525).

Data Collected

Demographic information, medical history, presenting symptoms, physical examination, electrocardiogram (ECG) readings, cardiac enzyme (creatine kinase–MB fraction [CK-MB]) measurements, 24-hour follow-up (including follow-up serum CK-MB tests and ECGs), and the final diagnosis were recorded for enrolled patients. When presenting clinical signs and symptoms were not recorded in the medical records as present, they were considered as negative for our analyses. The ECG variables were derived, as previously described,[26] from computerized-electrocardiograph measurements of the waveforms in the patient's initial ED electrocardiogram which classified Q, ST, and T wave changes if they were present in at least two contiguous leads.

Of the 10,525 ACI-TIPI Trial enrolles, 34 did not have their ethnic background recorded. In addition, the computer-derived variables from the initial ECGs were unavailable for 2,010 ED patients. The patients missing these ECG variable recordings were distributed among all of the study hospitals. The ECG variables and ethnic background variables were considered critical for our study analyses (see below); therefore, the analyses presented here were done on the 81% (N = 8,488) of patients with complete recorded data. Patient characteristics and results of univariate analyses performed on the entire study population (including the 19% excluded subjects) were similar to those obtained using the 81% of patients with complete data presented here.

Diagnosis of Acute Myocardial Infarction

For these analyses, the confirmed final diagnosis of AMI was based on the World Health Organization criteria,[27] which require two of three of the following: characteristic clinical presentation, elevated serum CK-MB levels, or diagnostic ECG findings.

Statistical Analyses

Univariate Analyses

Univariate comparisons used χ^2 tests for categorical variables and the Student's t test for continuous variables. In both cases, a 95% confidence level was chosen to assess statistical significance.

Logistic Regression Models

To assess gender effects on AMI prevalence while adjusting for patient characteristics, a logistic regression model was developed using SAS software version 6.10. Hospitals were forced into the model followed by stepwise inclusion of patient demographics, presenting signs and symptoms, and ECG features from the following variables: age in various forms (continuous and various grouping options were tested), chest pain, chief complaint of chest pain, shortness of breath, nausea or vomiting, computer-derived ECG variables (ST elevation, ST depression, Q wave presence), presence of CHF (pulmonary edema on chest x-ray or rales on examination), presence of dizziness, presence of abdominal pain, ethnic background, history of myocardial infarction, history of angina pectoris, history of diabetes mellitus, history of hypertension, history of peptic ulcer disease, and history of stroke (see Appendix A for further definition of the variables). Variables with p values $< .05$ were maintained in the model. After this model was developed, gender was forced into the model to assess its significance in determining AMI likelihood. Variables not initially included in the model were then retested for inclusion following the addition of gender. A logistic regression model was also devel-

oped giving gender as an initial selection variable, to compare with the above-described model.

The area under the receiver-operating characteristic (ROC) curve was used to estimate the discriminatory performance of the logistic regression model.[28] The final model was calibrated using 10 groups created by ranking all patients by their probability of AMI and dividing them into 10 groups of equal size. The mean observed probability of AMI and the mean of the model's predicted probability of AMI for the groups were compared using the Hosmer-Lemeshow statistic.[29]

To assess the robustness of the gender effect, the prediction model without gender was used to determine AMI likelihood, as a propensity score,[30] and then to rank patients accordingly. The patients were then divided into equal-sized quartiles of increasing AMI likelihood, and for each quartile a χ^2 analysis of gender and final diagnosis of AMI was performed.

All variables in the final logistic regression model were tested for statistically significant interaction with gender. All statistically significant ($p < .05$) interactions were further analyzed by subgrouping patients by gender and the variable in question, and determining the odds of AMI for the subgroups.

Analysis of Congestive Heart Failure and Comorbid Disease Relations

Although not fully diagnostic, the presence of rales on examination or pulmonary edema on chest roentgenogram or both in patients with symptoms of acute cardiac ischemia are suggestive of CHF. Therefore, in this article CHF is used to designate the presence of one or both of these findings. As CHF may result from damage to myocardium due to AMI or chronic comorbidities, specifically diabetes mellitus and hypertension,[31,32] we tested the interaction of these variables in predicting AMI. Our logistic regression model was used to test the various interaction pairs between history of diabetes mellitus, history of hypertension, and presence of CHF for statistical significance (95% confidence level).

RESULTS

Patient Characteristics

The characteristics of the 8,488 study patients for whom complete recorded data were available are shown in Table 1. Women comprised 49% of the study patients and were slightly older than the men (mean age 61 years, compared with 57 years in men). There was ethnic diversity among both genders, although the distributions of ethnic backgrounds were different. Chest pain was reported in 76% of men and 75% of the women and was more frequently the "chief complaint" in men. A higher percentage of women had nausea or vomiting, shortness of breath, and findings consistent with CHF (rales on examination or pulmonary edema on chest roentgenogram). Women's medical histories more often included hypertension and diabetes mellitus, while more men had histories of myocardial infarction, angina pectoris, and peptic ulcer disease. Men also more often had Q waves and ST-segment elevations on their ECG tracings. As noted above, 19% of study patients did not have electronic ECG recordings, but these were distributed among all the study hospitals with no noted gender bias ($p = .3$ for the χ^2 testing of missing ECG data by hospital and gender).

Prevalence of Acute Myocardial Infarction in Emergency Department Population

Among the presenting ED study patients, 10% of the men and 6% of the women had confirmed final diagnoses

Table 1. Study Patient Characteristics ($N = 8,488$)*

Patient Characteristic	Men ($n = 4,305$; 51%)	Women ($n = 4,183$; 49%)	p Value
Age, years	57	61	<.01
Ethnic background, %			
White	67	57	
African American	27	37	<.01
Other	5	6	
Presenting symptoms, %			
Chest pain	76	75	.13
Chief complaint of chest pain	69	66	<.01
Shortness of breath	53	56	<.01
CHF	22	25	<.01
Nausea/vomiting	25	31	<.01
Abdominal pain	12	13	.30
Dizziness	25	25	.87
Electrocardiographic findings, %			
ST-segment elevation			
None	86	95	
1 mm	11	4	<.01
2 mm or more	3	1	
ST-segment depression			
None	87	86	
0.5 mm	8	9	.03
1 mm	4	4	
2 mm	1	1	
Q-waves present	17	11	<.01
Medical history, %			
Myocardial infarction	30	21	<.01
Angina	36	34	.04
Stroke	8	9	.15
Diabetes mellitus	19	25	<.01
Hypertension	47	55	<.01
Peptic ulcer	15	14	.06

**Of the 10,525 patients enrolled in the study, 2,010 were missing computerized ECG readings and 34 were missing recording of ethnic background (7 were missing both). CHF indicates congestive heart failure.*

Table 2. Prevalence of Acute Myocardial Infarction Among Emergency Department Patients (*N* = 8,488)

Patient Group	Men, % (*n* = 4,305)	Women, % (*n* = 4,183)	*p* Value
All patients	10	6	<.01
Age subgroups by years (*n*)			
30–44 (1,886)	3	1	<.01
45–54 (1,624)	10	4	<.01
55–64 (1,593)	12	7	<.01
65–74 (1,756)	15	7	<.01
≥75 (1,629)	14	9	<.01

of AMI ($p \leq .01$). A male-to-female ratio of approximately 2:1 was consistently seen in the various age subgroups (Table 2).

Multivariable Logistic Regression Models

Given the differences in the patient characteristics between the men and women in our study, we wished to control for commonly recognized characteristics known to correlate with AMI presence and then determine if gender remained a significant AMI predictor. To do this we developed a multivariable logistic regression model predicting the confirmed diagnosis of AMI. The model was initially developed without gender as a potential variable. The model included age (> 50 years), chest pain as a symptom and as a chief complaint, ECG variables (ST elevation, ST depression, and Q waves), presence of nausea or vomiting, presence of CHF, presence of dizziness, ethnic background (dicotomized as white vs nonwhite), and histories of angina pectoris, peptic ulcer disease, and diabetes mellitus. In this initial model, history of hypertension was not included but was found to trend toward statistical significance (odds ratio [OR] 1.2; $p = .07$).

When gender was added to this model, it was found to be a statistically significant predictor of AMI with a male-to-female OR of 1.63 (95% confidence interval [CI] 1.36, 1.96). With gender in the model, retesting of the variables that were not initially included in the model resulted in the inclusion of history of hypertension (OR 1.2; $p = .03$). With the inclusion of this variable, gender remained significant (OR 1.66; 95% CI 1.38, 1.99). When a predictive model was developed using stepwise selection and including gender with the other variable choices, the same model was obtained.

The variables included in our model are listed in Appendix B (explanation of the addition of the interaction terms is described below). The model had a ROC curve area of 0.833 reflecting excellent discriminatory performance and was well calibrated based on the Hosmer-Lemeshow analysis (see Figure 1). Negative coefficients for history of angina, history of peptic ulcer disease, and dizziness most likely reflect the broad inclusion criteria used to enroll patients in the study. As this was a model to control maximally for presentation, we have retained these

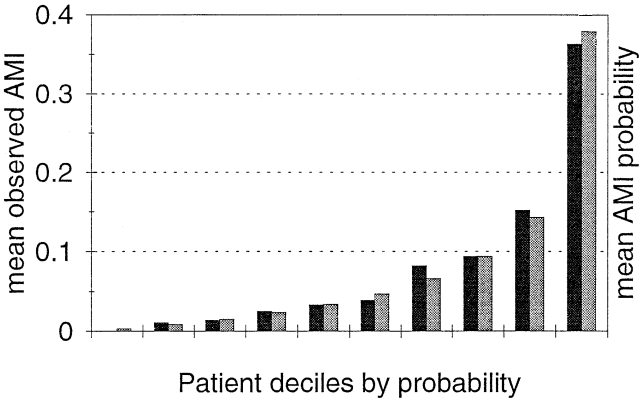

FIGURE 1. Model performance and calibration. ROC area = 0.833. Hosmer-Lemeshow analysis: $\chi^2 = 9.27$ ($df = 8$); not statistically significant ($p = .32$). Patients were ranked by the AMI probability (as determined using the logistic regression model presented in Appendix B) and divided into 10 equal groups. The lighter shaded bars represent the mean estimated AMI probabilities for each of the 10 groups. The darker bars represent the observed proportions of AMI for each of these same groups.

variables in the model. When these variables were removed from the model, its predictive capability, as assessed by ROC area (0.83) and calibration (Hosmer-Lemeshow $\chi^2 = 4.5$, $df = 8$) were similar.

To assess the robustness of the gender effect for different probabilities of AMI, the gender variable was removed from the model and the remaining model was used as a propensity score (ROC area = 0.825) for AMI probability. The patients were ranked by their probability scores (ranging from 0 to 0.97) and divided into quartiles. Given the low AMI prevalence, these quartiles represented AMI probabilities of <0.01, 0.01–0.05, 0.05–0.10, and >0.10. Gender was tested in each quartile. Similar increased risk was seen in each quartile (OR 2.2, 95% CI 0.2, 23.8; OR 1.7, 95% CI 1.1, 2.7; OR 1.7, 95% CI 1.2, 2.4; and OR 1.7, 95% CI 1.3, 2.1; respectively), although statistical significance was not found in the lowest quartile (AMI probability < 1%). When the upper quartile was further divided, gender remained significant in both the lower two thirds (probability of AMI from 10% to 25%) and the upper one third (AMI probability > 25%) with OR of 1.7 (95% CI 1.2, 2.3) and OR of 1.4 (95% CI 1.0, 2.0), respectively.

The possibility of significant differences in the gender effect between participating hospitals was tested for, and no statistically significant global interaction was found (likelihood ratio $\chi^2 = 10.0$; $df = 9$).

Gender–Variable Interactions

All variables in the final model were tested for interaction with the gender variable. Significant interactions were found with presence of CHF, presence of ST elevations on ECG, and ethnic background recorded as white. These interactions were included in our final model (Ap-

pendix B). As a gender interaction signified a differential effect of the variable on AMI likelihood among women and men, we wished to clarify these differences further.

The three variables with statistically significant interactions with the gender variable were further explored through the subgrouping of patients by both gender and each of the three variables. For each, we determined the likelihood of AMI for each subgroup after controlling for the other variables in our logistic regression model. The results are shown in Table 3 for the presence of CHF, ST elevation on ECG, and white ethnic background.

In our multivariable model we found that the odds for AMI were similar for *men with CHF, men without CHF,* and *women with CHF*. Each of these groups had a statistically significant OR of approximately 2 relative to *women without CHF* (Table 3). Among patients with signs of CHF, the likelihood of AMI was similar for men and women (OR 1.1; 95% CI 0.8, 1.5).

We found a very large increase in AMI likelihood with ST elevation in both men and women (Table 3). However, there was also a higher AMI likelihood in men without ST elevations as compared with women without ST elevations (OR 1.9; 95% CI 1.5, 2.3). The overall gender interaction reflected the incrementally greater increase in likelihood in women with ST elevations as compared with those without. Within the subgroup of patients with ST elevations (which was 10% of the study population and represented 30% of the AMI patients), after controlling for the other model variables, gender was no longer significant (OR 1.1; 95% CI 0.7, 1.7).

The results of the subgroup analyses of the gender interaction with ethnic background (white vs nonwhite) suggested that the gender interaction reflects a differential effect of white versus nonwhite ethnic background among men (Table 3). No significant difference in AMI likelihood is noted between white versus nonwhite women or between nonwhite men and women.

Table 3. Subgroup Analyses of Gender–Variable Interactions

Interaction	Odds Ratio (95% CI)	*p* Value
Gender–CHF: reference, women without CHF		
Men with CHF	2.0 (1.5, 2.7)	<.01
Men without CHF	2.1 (1.6, 2.6)	<.01
Women with CHF	1.9 (1.4, 2.5)	<.01
Gender–ST-segment elevation: reference, women without elevated ST		
Men with elevated ST	12.8 (9.7, 17.0)	<.01
Men without elevated ST	1.9 (1.5, 2.3)	<.01
Women with elevated ST	11.5 (8.1, 16.5)	<.01
Gender–ethnicity: reference, nonwhite women		
White men	2.2 (1.6, 2.9)	<.01
Nonwhite men	1.1 (0.8, 1.6)	.5
White women	1.1 (0.8, 1.6)	.4

Congestive Heart Failure–Comorbid Disease Relations

One explanation for the differential effect of CHF in women was the possibility that it resulted from underlying myocardial damage, not solely due to coronary artery disease but due to or associated with chronic comorbid diseases. In particular, we considered diabetes mellitus and hypertension, which were more prevalent in women (Table 1). This was checked by testing for statistically significant interactions. When interactions between presence of CHF, history of hypertension, and history of diabetes mellitus were analyzed in our model, no statistically significant interactions were found. The same was true when the models were tested separately on men and women. History of diabetes mellitus and history of hypertension appeared to be somewhat stronger predictors of AMI in the symptomatic women as compared with the men (Table 4).

Statistically, these three variables appear to be independent predictors of AMI, and therefore the AMI likelihood would be increased for each characteristic present. Among the women in this ED population of symptomatic patients, of those with CHF, 8% also had diabetes mellitus, 38% had hypertension, and 30% had both diabetes mellitus and hypertension. Of women with CHF who had final diagnoses of AMI, 8% had diabetes mellitus, 36% had hypertension, and 39% had both diabetes mellitus and hypertension.

Table 4. Likelihood of Acute Myocardial Infarction in Women and Men with Congestive Heart Failure, History of Diabetes Mellitus, or History of Hypertension

	Men	Women
Variable	Odds Ratio (95% CI)*	Odds Ratio (95% CI)*
CHF	1.0 (0.8, 1.3)	1.9 (1.4, 2.6)
Diabetes mellitus history	1.2 (0.9, 1.6)	1.5 (1.1, 2.1)
Hypertension history	1.2 (0.9, 1.5)	1.3 (1.0, 1.9)

**Adjusted odds ratios and 95% confidence intervals are derived from the logistic regression model in Appendix B for men and women separately. No significant interactions between these variables were found in either men or women.*

DISCUSSION

This study examined the prevalence of AMI in men and women who presented to EDs with chest pain or other symptoms suggestive of acute cardiac ischemia. Among these patients, men had an approximately twofold higher prevalence of AMI overall and in all age subgroups, compared with women. Several population-based studies have reported an increased overall incidence of AMI in men[11–14]; in the Framingham study, this male-to-female ratio was 10:1 in patients under 45 years old, dropping progressively to approximately 2:1 in patients over 75 years old.[11] Symptoms that suggest AMI are often what prompt a patient with AMI to visit the ED; therefore, one might have expected the population-based gender difference in AMI prevalence to be eliminated in this select population. However, the gender difference appears to persist even among these symptomatic ED patients.

To understand the basis for this observed difference in AMI prevalence between genders, we considered several possible underlying factors. First, the differences could be the result of study inclusion criteria. Previous studies have used the specific presenting symptom of chest pain as a criterion for patient inclusion, and have reported lower rates of AMI in women than in men.[2,18,24] However, retrospective analyses of AMI patients have suggested that women have "atypical presentations" (non–chest pain) more often than men.[11,20–23] In contrast to previous studies, a broader ED patient population was enrolled in our study: 24% of the men and 25% of the women were enrolled due to non–chest pain symptoms. Nonetheless, the higher prevalence of AMI among the men persisted.

Although all patients in our study had symptoms suggestive of acute cardiac ischemia, the clinical presentations differed somewhat between the women and men. Therefore, we examined whether the gender difference in the likelihood of AMI persisted after adjusting for the patient's prominent presenting characteristics using a multivariable logistic regression model. Age greater than 50, computer-derived ECG variables, and presence of chest pain have been shown to be predictors of acute cardiac ischemia in a validated predictive instrument.[33] Our model predicting AMI included these variables as well as the presence of nausea or vomiting, ethnicity, the presence of CHF (i.e., pulmonary edema on chest x-ray or rales on examination), and histories of two cardiac risk factors, diabetes mellitus and hypertension. In addition, three variables were included in the model with negative coefficients: history of peptic ulcer disease, history of angina, and presence of dizziness. These inclusions most likely reflect the study's broad inclusion criteria rather than truly signifying "protective characteristics." Because we were developing the model to control for patient presentation, these variables were left in our model.

After adjusting for the prominent presenting characteristics, gender remained a significant factor in determining a patient's AMI likelihood, with a male-to-female ratio of 1.7. These results concur with previous epidemiologic studies of gender differences in both development and expression (AMI vs angina pectoris) of coronary artery disease.[11,24] When the model (with gender removed) was used to stratify patients by probability of AMI, male gender appeared to increase AMI likelihood in all quartiles. The lack of statistical significance in the lowest quartile of patients (< 1% probability of AMI) may reflect a low power for detection due to low AMI prevalence or may support a lack of gender bias in the study enrollment.

We recognize that logistic regression model development using a stepwise procedure is influenced by the candidate variables. However, our use of broad inclusion criteria for symptoms suggestive of acute cardiac ischemia (not limited to chest pain), the finding that our model was robust, and the similarity of the variables in our model to those in the validated acute cardiac ischemia predictive instruments,[33,34] helped to increase confidence in our multivariable model. Further testing is needed to assess its utility as a predictive model.

The persistence of a gender difference in the prevalence of AMI noted in our study concurred with the results from a published study of ED patients with chest pain.[18] In that report, after controlling for 22 presenting characteristics, gender was found to be a significant factor in AMI prevalence (male-to-female risk ratio of 1:6). However, among the subgroup of patients with nonblinded, ED physician–read "classic electrocardiographic changes of infarction," the gender difference was not found. In our study, using uniform, objective (and blinded) computer-derived measures of ECG changes, similar results were found for patients with ST-segment elevations (for male gender: OR 1.1; 95% CI 0.7, 1.7). It is important to recall, however, that ST elevations were present in only 30% of the AMI patients in our study population. For the remaining 70%, gender remained a significant predictor of AMI.

The multivariable model helped us to assess gender-specific presenting characteristics related to AMI in men or women. We found a statistically significant interaction between gender and white ethnic background. However, since age, gender, and other patient characteristics differ among the ethnic groups, further investigation is needed to understand this statistical interaction and to determine its clinical significance, if any.

An interaction was also found between gender and the presence of CHF. The presence of CHF was a more significant predictor of increased AMI likelihood in women than in men. In the female ED patients, the presence of CHF increased their AMI likelihood to the same level as that in men (both with or without CHF). This finding paralleled reports that women present with higher Killip class AMIs than men,[22,23,35] and that among patients with AMI, women have a higher prevalence of CHF.[11,15,22]

The presence of CHF may signify underlying worsened cardiac status, perhaps due to comorbidities, which may result in increased development of infarction from an episode of cardiac ischemia. Alternatively, the presence of

CHF may be the manifestation of AMI in a patient with previous underlying cardiac compromise (such as diastolic dysfunction) and as such may be a marker of AMI. Our study results could not distinguish between these mechanisms of cause or effect. This difference in AMI prevalence between patients with and without CHF was seen among women but not among men, and as such may represent distinct or more prevalent female processes in AMI development.

Diabetes mellitus and hypertension have been shown to increase the risk of coronary artery disease and to increase the risk of CHF[32,36–38]; however, in the symptomatic women in our ED population, the increased AMI likelihood due to these comorbidities appeared to be independent of the increased AMI likelihood due to CHF. Increased AMI likelihood for patients with a history of diabetes mellitus or a history of hypertension appeared to be somewhat greater among the women in our study as compared with the men (Table 4) although no statistically significant gender interactions were found. These differences noted in the separate analyses of men and women may in part reflect the higher prevalence of comorbid disease histories among the women. The increased prevalence of these comorbid diseases among symptomatic women has been reported,[15,22,23,39–41] and is not solely a reflection of their prevalence among women in the general population.[42,43]

Although further study is needed to better understand the relations of these comorbid diseases and the presence of CHF to AMI likelihood in women, it is important to recognize the high rate of coexistence of these factors (particularly of the presence of CHF and a history of hypertension) and the further increased likelihood of AMI in the symptomatic women with these characteristics.

In summary, in men and women presenting to the ED with symptoms suggestive of acute cardiac ischemia, the prevalence of AMI is approximately twofold higher in men than in women after controlling for presenting characteristics. The presence of ST-segment elevations on ECG dramatically increased AMI likelihood in both men and women, eliminating the gender difference. In the subgroup of women with symptoms suggestive of acute cardiac ischemia and *presence of CHF*, the prevalence of AMI is increased to equal that in men (either with or without CHF). This suggests that independent of the increased AMI risks due to histories of diabetes mellitus or hypertension, the presence of CHF should be given substantial weight in assessing the likelihood of AMI in women presenting to the ED with symptoms suggestive of acute cardiac ischemia.

We thank Robin Ruthazer, MPH, for her statistical and programming assistance and for helpful discussions.

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APPENDIX A
Definitions of Variables in Logistic Regression Model Predicting Confirmed Diagnosis of Acute Myocardial Infarction

Variable Names*	Definition
Gender	1 = Male 0 = Female
Age<50	Age<50 = (age in years)−30 Age≥50 = 20
Chest pain	1 = Complaint of chest pain or discomfort 0 = No complaint of chest pain
CC: chest pain	1 = "Chief complaint" of chest pain or discomfort 0 = "Chief complaint" not chest pain
Nausea/vomit	1 = Patients with nausea and/or vomiting 0 = Patients without nausea or vomiting
CHF	1 = Rales on exam and/or pulmonary edema on ED chest x-ray 0 = No recorded rales on exam or pulmonary edema on chest x-ray
White	1 = Ethnic background recorded as white 0 = Ethnic background recorded as other than white
African American	1 = Ethnic background recorded as African American 0 = Ethnic background recorded as other than African American
ST elevation*	2 = ST elevation of 0.2 mV or more 1 = ST elevation of 0.1–0.199 mV 0 = No significant ST elevation
ST depression*	2 = ST depression of 0.2 mV or more 1 = ST depression of 0.1–0.199 mV 0.5 = ST depression of 0.05–0.099 mV 0 = No significant ST depression
Q waves*	1 = Abnormal Q waves present 0 = If otherwise
Shortness of breath	1 = Presence of shortness of breath 0 = No record of shortness of breath
Abdominal pain	1 = Presence of abdominal pain 0 = No recorded presence of abdominal pain
Dizziness	1 = Presence of dizziness 0 = No recorded presence of dizziness
History of myocardial infarction	1 = History of myocardial infarction 0 = No recorded history of myocardial infarction

continued

APPENDIX A
Continued

Variable Names*	Definition
History of angina	1 = History of angina pectoris 0 = No recorded history of angina pectoris
History of stroke	1 = Recorded history of stroke 0 = No recorded history of stroke
History of peptic ulcer disease	1 = History of peptic ulcer disease 0 = No recorded history of peptic ulcer disease
History of diabetes mellitus	1 = History of diabetes 0 = No recorded history of diabetes
History of hypertension	1 = History of hypertension 0 = No recorded history of hypertension
Interactions	Product of the noted variables

** Variables assess presence of waveform abnormalities if present in at least two contiguous leads.[26]*

APPENDIX B
*Variables in Logistic Regression Model Predicting Confirmed Diagnosis of Acute Myocardial Infarction**

Variable Names	Coefficients†	p Value
Gender	0.4852	.02
Age<50	0.1432	<.01
Chest pain	0.8792	<.01
CC: chest pain	0.4399	.02
Nausea/vomit	0.5153	<.01
CHF	0.6759	<.01
White	0.0987	.6
ST elevation‡	2.0948	<.01
ST depression‡	1.2632	<.01
Q waves‡	0.5311	<.01
History of diabetes mellitus	0.2781	<.01
History of hypertension	0.2032	.04
History of angina	−0.2976	<.01
History of peptic ulcers	−0.3210	.02
Dizziness	−0.4437	<.01
Interactions§		
Gender and CHF	−0.6899	<.01
Gender and ST elevation	−0.5187	<.01
Gender and white	0.5206	.02

continued

APPENDIX B
Continued

** Variables were chosen from the options described in the Methods section; for definitions see appendices.*
† Reported coefficients are adjusted for hospitals.
‡ Variables assess presence of waveform abnormalities if present in at least two contiguous leads.[26]
§ Each interaction is the product of the two listed variables, where gender = 1 for men, presence of CHF = 1, presence of ST elevations on ecg = 1 and ethnic background recorded as white = 1. Therefore, the interaction terms refered to men with CHF, men with ST elevations on ecg and men with their ethnic background recorded as white, respectively.